

CLAIMS

1. A method for electronically detecting at least one specific interaction between probe molecules fixed to at least one active zone of a sensor and target biomolecules, characterized in that said sensor consists of an array of field-effect transistors ( $T_1$ ,  $T_2$ , etc.), each of which has a source region (5), a drain region (D), and a gate region which constitutes an active zone (3) on which said specific interaction is to be detected, and in that it comprises the following steps:
- a) bringing at least one active zone (3) into contact with probe molecules of a given type fixed to said active zone,
  - b) bringing at least some of the probe molecules into contact with target biomolecules capable of interaction with said probe molecules, and performing a said interaction in a reaction buffer having a first salt concentration,
  - c) measuring at least one point of the drain current/source-gate voltage/source-drain voltage characteristic of at least one transistor of said array to detect said specific interaction at least for a measurement point obtained in a measuring buffer having a second salt concentration that is lower than the first concentration for probe molecules having been subjected to said specific interaction.
2. The method as claimed in claim 1, characterized in that said measurement is carried out by means of a difference between said measurement point and a reference point, in particular in a said measuring buffer, for probe molecules that have not been subjected to a specific interaction.
3. The method as claimed in claim 2, characterized in

that said reference point is determined from probe molecules of the same type as those that were subjected to said specific interaction, and having even the same sequence or a different sequence.

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4. The method as claimed in either of claims 2 or 3, characterized in that the differential measurement of step c) is carried out on two groups of probe molecules fixed to distinct active zones (3), the probe  
10 biomolecules of one of the groups having been subjected to the interaction of step b), and not the other.

5. The method as claimed in claim 1, characterized in that step c) is carried out differentially between two  
15 measurement points obtained in a said measuring buffer for probe molecules having been subjected to two different interactions.

6. The method as claimed in claim 5, characterized in  
20 that the probe molecules subjected to said two different interactions are of the same type, whether or not they have identical sequences.

7. The method as claimed in claim 5, characterized in  
25 that said differential measurement of step c) is carried on two groups of probe molecules fixed to distinct active zones (3), the probe molecules of one of the groups having been subjected to said specific interaction and the probe molecules of the other group  
30 having been subjected to another specific interaction.

8. The method as claimed in either of claims 2 and 3, characterized in that the differential measurement of step c) is carried out on the same probe molecules  
35 before and after they are subjected to said interaction during step b).

9. The method as claimed in one of the preceding claims, characterized in that said measurement of at

least one point of the characteristic uses the application of a given voltage ( $U_{DS}$ ) between the drain and the source of at least one transistor, and also the application, in a first case, of a given voltage ( $U_{GS}$ )  
5 between the gate and the source of said transistor or, in a second case, of a given drain current ( $I_D$ ), to said transistor.

10. The method as claimed in claim 9, characterized in  
10 that, in the first case, the point is obtained by measuring the drain current  $I_D$  and, in the second case, by measuring the voltage  $U_{GS}$  between the gate and the source.

15 11. The method as claimed in one of the preceding claims, characterized in that the measuring buffer is KCl.

20 12. The method as claimed in one of the preceding claims, characterized in that the concentration of the reaction buffer is between 20 mM and 1 M.

25 13. The method as claimed in claim 12, characterized in that the concentration of the measuring buffer is greater than 0.002 mM and less than 20 mM.

30 14. The method as claimed in claim 13, characterized in that the concentration of the measuring buffer is at least equal to 0.01 mM.

15. The method as claimed in either of claims 13 and 14, characterized in that the concentration of the measuring buffer is at most equal to 15 mM.

35 16. The method as claimed in one of the preceding claims, characterized in that the passage between one buffer and a buffer of lower concentration is separated by a rinsing step.

17. The method as claimed in one of the preceding claims, characterized in that the probe molecules are molecules, in particular biomolecules, capable of being recognized by a type of target biomolecule.

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18. The method as claimed in claim 17, characterized in that the probe molecules and/or the target biomolecules are DNA, RNA or protein molecules, or else vitamins.

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19. The method as claimed in claim 18, characterized in that the probe biomolecules are DNA molecules and in that the field-effect transistors are of the depleted n-channel type, with a negative gate bias.

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20. The method as claimed in one of the preceding claims, characterized in that it comprises, before a), at least one control measurement step with a said measuring buffer.

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21. The method as claimed in one of the preceding claims, characterized in that it comprises the circulation of at least one solution which constitutes a reference or which contains target molecules through at least one microfluidic channel so as to bring it into contact with at least one said field-effect transistor.

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